=> file uspat

=> e left cobalamin
E1 1 COBALAMIDES/BI
E2 1 COBALAMIIN/BI
E3 212 --> COBALAMIN/BI
E4 31 ADENOSYLCOBALAMIN/BI
E5 9 ADENOSYLCYANOCOBALAMIN/BI
E6 1 ADENSOSYLCOBALAMIN/BI
E7 8 AQUACOBALAMIN/BI
E8 15 AQUOCOBALAMIN/BI
E9 1 ASCYANOCOBALAMIN/BI
E10 3 BENZIMIDAZOLECYANOCOBALAMIN/BI
E11 1 BENZYLCOBALAMIN/BI
E12 9 CHLOROCOBALAMIN/BI

=> s ?cobalamin?
L1 1259 ?COBALAMIN?

=> s conjugat?
L2 65801 CONJUGAT?

=> s l1(6a)l2
L3 21 L1(6A)L2

=> d bib kwic

L3 ANSWER 1 OF 21 USPATFULL
AN 2001:17971 USPATFULL
TI Transcobalamin mediated transport of vitamins B12 in intrinsic factor or receptor deficient patient
IN Seetharam, Bellur, Brookfield, WI, United States
Bose, Santanu, San Francisco, CA, United States
PA MCW Research Foundation, Milwaukee, WI, United States (U.S. corporation)
PI US 6183723 20010206
AI US 1998-9995 19980121 (9)
DT Utility
EXNAM Primary Examiner: Saucier, Sandra E.; Assistant Examiner: Afremova, Vera
LREP Quarles & Brady LLP
CLMN Number of Claims: 1

ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 6 Dra·ving Page(s)
LN.CNT 969
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . inactivated prior to absorption or is not absorbed. In one embodiment a hydrophobic drug, preferably a synthetic organic molecule, is ***conjugated*** to a ***cobalamin*** molecule. The ***cobalamin*** drug ***conjugate*** is then bound to ***transcobalamin*** II and an effective amount is orally delivered to the patient.
SUMM The ***cobalamin*** /drug ***conjugate*** bound to ***transcobalamin*** II will be transcytosed from the intestinal lumen to circulation as an intact complex. The complex present in the circulation. . .
SUMM In another embodiment of the present invention, a drug is ***conjugated*** directly to a ***transcobalamin*** II molecule and an effective amount is orally delivered to the patient.
DETD . . . II. The initial biotin-Cbl complex can be prepared according to Pathre, et al. (Pathre, P. M., et al., "Synthesis of ***Cobalamin*** -Biotin ***conjugates*** that vary in the position of ***cobalamin*** coupling, Evaluation of cobalamin derivative binding to transcobalamin II," incorporated by reference).

=> s boron
L4 86436 BORON

=> s l3 (L)l4
L5 5 L3 (L)L4

=> d bib,kwic

L5 ANSWER 1 OF 5 USPATFULL
AN 1999:132802 USPATFULL
TI 1 .alpha.-hydroxy-25-ene-vitamin D, analogs and uses thereof
IN Bishop, Charles W., 5 LaPointe Ter., Madison, WI, United States 53719
Knutson, Joyce C., 24 N. Prospect Ave., Madison, WI, United States 53705
Strugnell, Stephen, 2622 Dahle St., Madison, WI, United States 53704
PI US 5972917 19991026
AI US 1998-87439 19980529 (9)
DT Utility
EXNAM Primary Examiner: Criares, Theodore J.

=> s l3 not l4
L6 16 L3 NOT L4

=> d bib,kwic 1-16

L6 ANSWER 1 OF 16 USPATFULL
AN 2001:17971 USPATFULL
TI Transcobalamin mediated transport of vitamins B12 in intrinsic factor or receptor deficient patient
IN Seetharam, Bellur, Brookfield, WI, United States
Bose, Santanu, San Francisco, CA, United States
PA MCW Research Foundation, Milwaukee, WI, United States (U.S. corporation)
PI US 6183723 20010206
AI US 1998-9995 19980121 (9)
DT Utility
EXNAM Primary Examiner: Saucier, Sandra E.; Assistant Examiner: Afremova, Vera
LREP Quarles & Brady LLP
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 969
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . inactivated prior to absorption or is not absorbed. In one embodiment a hydrophobic drug, preferably a synthetic organic molecule, is ***conjugated*** to a ***cobalamin*** molecule. The ***cobalamin*** drug ***conjugate*** is then bound to ***transcobalamin*** II and an effective amount is orally delivered to the patient.
SUMM The ***cobalamin*** /drug ***conjugate*** bound to ***transcobalamin*** II will be transcytosed from the intestinal lumen to circulation as an intact complex. The complex present in the circulation. . .
SUMM In another embodiment of the present invention, a drug is ***conjugated*** directly to a ***transcobalamin*** II molecule and an effective amount is orally delivered to the patient.
DETD . . . II. The initial biotin-Cbl complex can be prepared according to Pathre, et al. (Pathre, P. M., et al., "Synthesis of ***Cobalamin*** -Biotin ***conjugates*** that vary in the position of ***cobalamin*** coupling, Evaluation of cobalamin derivative binding to transcobalamin II," incorporated by reference).

L6 ANSWER 2 OF 16 USPATFULL

AN 2000:84267 USPATFULL
TI Water soluble vitamin B.sub.12 receptor modulating agents and methods related thereto
IN Morgan, Jr., A. Charles, Mill Creek, WA, United States
Wilbur, D. Scott, Edmonds, WA, United States
Pathare, Pradip M., Seattle, WA, United States
PA The University of Washington, Seattle, WA, United States (U.S. corporation)
Receptagen Corporation, Edmonds, WA, United States (U.S. corporation)
PI US 6083926 20000704
AI US 1998-200422 19981123 (9)
RLI Division of Ser. No. US 1995-545151, filed on 19 Oct 1995, now patented, Pat. No. US 5840712 which is a continuation-in-part of Ser. No. WO 1995-US4404, filed on 7 Apr 1995 which is a continuation-in-part of Ser. No. US 1995-406191, filed on 16 Mar 1995, now patented, Pat. No. US 5840880 which is a continuation-in-part of Ser. No. US 1995-406192, filed on 16 Mar 1995, now patented, Pat. No. US 5739287 And a continuation-in-part of Ser. No. US 1995-406194, filed on 16 Mar 1995, now patented, Pat. No. US 5869465 which is a continuation-in-part of Ser. No. US 1994-224831, filed on 8 Apr 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Fonda, Kathleen K.
LREP Seed Intellectual Property Law Group PLLC
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 3274
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD . . . a graph illustrating the binding curve of Transcobalamin II to the cyanocobalamin diaminododecane adducts produced in Example 3 and 4. AH= ***Cyanocobalamin*** b-monocarboxylic acid ***conjugate*** diaminododecane (7); AI= ***Cyanocobalamin*** e-monocarboxylic acid ***conjugate*** diaminododecane (8); AJ= ***Cyanocobalamin*** d-monocarboxylic acid ***conjugate*** diaminododecane (9); AK= ***Cobalamin*** e-monocarboxylic acid ***conjugate*** diaminododecane, and AE= ***Cyanocobalamin*** ribose-succinate (11).
DRWD . . . 25 is a graph illustrating the binding curve of Transcobalamin II to a series of biotinylated vitamin B.sub.12 molecules. AA ***Cyanocobalamin*** b-monocarboxylic acid ***conjugate*** diaminododecane and biotin (17); AB= ***Cyanocobalamin*** e-monocarboxylic acid ***conjugate*** diaminododecane and biotin (18); AC= ***Cyanocobalamin*** d-monocarboxylic acid ***conjugate*** diaminododecane and biotin (19); AF=

Cyanocobalamin ribose-succinate ***conjugate*** diaminododecane (13); and AG= ***Cyanocobalamin*** ribose-succinate ***conjugate*** diaminododecane and biotin (20). These biotinylated molecules were prepared as set forth in Examples below. (see Example 8.)

DETD ***Cyanocobalamin*** Modified on Ribose: Succinate ***Conjugate*** (5)

DETD . . . by phenol extraction and applied to a 100 g of Dowex Cl.sup.-(60.times.2.5 cm) column (acetate form, 200-400 mesh). The ***cyanocobalamin*** was eluted with water. Succinate ***conjugate*** (5) was eluted with NaOAc (0.04 M, pH 4.67) which yielded 180 mg (85%) after isolation. The O2',O5'-disuccinyl derivative remained. . .

DETD ***Cyanocobalamin*** Modified on Ribose: Succinate-diaminododecane ***Conjugate*** (13)

DETD Modification of ***Cyanocobalamin*** Monocarboxylic Acids ***Conjugated*** With 1,.sub.12 -diaminododecane: Reaction With Succinic Anydride

DETD ***Cyanocobalamin*** carboxylic acid diaminododecane ***conjugate*** (8, 9, 10) (0.138 mmoL, 200 mg) was dissolved in 40 mL of dimethylsulfoxide (DMSO) containing 8 g (80 mmoL). . .

DETD ***Cyanocobalamin*** Modified on Monocarboxylic Acid: Diaminododecane-biotin ***Conjugates***

DETD To a solution of ***cyanocobalamin*** monocarboxylic acid diaminododecane ***conjugate*** (14, 15, 16) (300 mg, 0.195 mmoL) in DMF (35 mL), was added triethylamine (0.027 mL, 0.195 mmoL). N-Hydroxysuccinimidobiotin (100. . .

DETD ***Cyanocobalamin*** Modified On Ribose: Succinate-diaminododecane-biotin ***Conjugate*** (20)

DETD This example serves to demonstrate the conjugation of the ribose-linked diaminododecane adduct (13) with biotin to produce a ***cyanocobalamin*** biotin ***conjugate*** (20).

DETD This example demonstrates coupling of streptomycin to a ***cyanocobalamin*** or ***cobalamin*** derivative. Streptomycin (21) is ***conjugated*** with ***cyanocobalamin*** monocarboxylate (2, 3, 4) or a diaminoalkylsuccinate derivative (14, 15, 16) through the use of an oxime coupled linking moiety. . .

DETD . . . reaction scheme illustrated in FIG. 14, method A, or similarly as described in method B. Both reaction schemes produce a ***cyanocobalamin*** -acridine ***conjugate*** .

DETD . . . yield the aminoacridine, (29). Aminoacridine (29) is then conjugated with vitamin B.sub.12 monocarboxylic acid (2, 3, 4) to yield a ***cyanocobalamin*** -acridine ***conjugate*** (30).

DETD . . . and evaporated to dryness. The residue was digested with 100 mL

of acetone and the solvent was decanted yielding a ***cyanocobalamin*** -acridine ***conjugate*** (32). Yield: .sub.12 0 mg (62%). mp 182-188.degree. C.

DETD This example demonstrates ***conjugation*** of amikacin to a ***cyanocobalamin*** molecule to form a ***cyanocobalamin*** -amikacin ***conjugate*** . A reaction scheme for the conjugation is depicted in FIG. 12. As noted above, chemical moieties that are retained subcellularly. . . Chemical Co., St. Louis), is reacted with a vitamin B.sub.12 monocarboxylate (2, 3, 4) in the presence of EDC. A ***cyanocobalamin*** -amikacin ***conjugate*** (34) is then separated and purified by reverse-phase LC chromatography under conditions noted above.

DETD ***Cyanocobalamin*** Monocarboxylic Acid Diaminododecane ***Conjugate*** Dimer: Isophthaloyl Dichloride Cross-linking

DETD To a solution of ***cyanocobalamin*** monocarboxylic acid diaminododecane ***conjugate*** (8, 9, 10) (0.192 mmol, 0.300 g) in DMF (30 mL), was added triethylamine (18 .mu.L). Isophthaloyl dichloride (35) (0.096. . .

DETD ***Cyanocobalamin*** Monocarboxylic Acid Diaminododecane ***Conjugate*** Dimer: ETAC Cross-linking

DETD ***Cyanocobalamin*** Monocarboxylic Acid Diaminododecane ***Conjugate*** Dimer: Isophthlate Cross-linking With Biotin Moiety

DETD Reaction Step F: In a solution of ***cyanocobalamin*** carboxylic acid-diaminododecane ***conjugate*** (8, 9, 10) (0.130 mmol, 0.2 g) in a mixture of DMF: H.sub.2 O (3:1) (40 mL) triethylamine (12 .mu.L). . .

DETD ***Cyanocobalamin*** Monocarboxylic Acid Diaminododecane ***Conjugate*** Dimer: Isophthalate Cross-linking With Para-iodobenzoyl Moiety

DETD Reaction Step C: To a solution of ***cyanocobalamin*** carboxylic acid-diaminododecane ***conjugate*** (56) (0.192 mmol, 0.3 g) in a mixture of DMF: H.sub.2 O (3:1) (40 mL) was added triethylamine (0.018 mL).. . .

DETD ***Cyanocobalamin*** Monocarboxylic Acid Diaminododecane ***Conjugate*** Dimer: Isophtahate Cross-linking With Para-(tri-butylstannyl)benzoyl Moiety

DETD Reaction Step B: In a solution of ***cyanocobalamin*** carboxylic acid-diaminododecane ***conjugate*** (8, 9, 10) (0.065 mmol, 0.1 g) in a mixture of DMF: H.sub.2 O (3:1) (40 mL) triethylamine (0.006 mL). . .

DETD . . . Diaminododecane (7); AI=Cyanocobalamin e-monocarboxylic acid conj Diaminododecane (8); AJ=Cyanocobalamin d-monocarboxylic acid conj Diaminododecane (9); AK=Cobalamin e-monocarboxylic acid conj

Diaminododecane, and AE= ***Cyanocobalamin*** Ribose-Succinate (11). The b- ***conjugate*** (17) has the least binding, whereas the e-conjugate (18) has intermediate binding, and the d-conjugate (19) binds quite well. The. . .

DETD In a solution of ***cyanocobalamin*** monocarboxylic acid trioxadiamine ***conjugate*** (0.193 mmol, 300 mg) in DMF (10 mL), triethylamine (0.193 mmol, 0.027 mL) was added. N-hydroxysuccinimidobiotin (0.232 mmol 79 mg). . .

DETD A. Isophthaloyl crosslinked dimer. The preparation and results for crosslinking using isophthaloyl dichloride and the b-isomer of ***cyanocobalamin*** monocarboxylic acid trioxadiamine ***conjugate*** are presented. The reaction product for the e-isoma is shown below. ##STR35##

DETD In a solution of ***cyanocobalamin*** monocarboxylic acid trioxadiamine ***conjugate*** (0.193 mmol, 0.300 g) in DMF (20 mL), triethylamine (0.030 mL) was added. Isophthaloyl dichloride (0.096 mmol, 0.0195 g) was. . .

DETD In a solution of ***cyanocobalamin*** carboxylic acid-trioxadiamine ***conjugate*** (0.193 mmol, 0.3 g) in DMF (15 mL), triethylamine (0.030 mL) was added. DiTFP ester of Biotin-caproic acid-Isophthalic acid (0.0965. . .

L6 ANSWER 3 OF 16 USPATFULL
AN 1999:19129 USPATFULL
TI Methods of receptor modulation and uses therefor
IN Morgan, Jr., A. Charles, Edmonds, WA, United States
Wilbur, D. Scott, Edmonds, WA, United States
PA Receptagen Corporation, Edmonds, WA, United States (U.S. corporation)
University of Washington, Seattle, WA, United States (U.S. corporation)
PI US 5869465 19990209
AI US 1995-406194 19950316 (8)
RLI Continuation-in-part of Ser. No. US 1994-224831, filed on 8 Apr 1994, now abandoned
DT Utility
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Gupta, Anish
LREP Christensen O'Connor Johnson & Kindness PLLC
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 2882
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD ***Cyanocobalamin*** Modified on Ribose: Succinate ***Conjugate*** (5)